CardioRenal Syndromes

By

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Cardio-Renal Syndromes

Classic view: CRS means that a normal kidney may be dysfunctional because of a diseased heart.

In the presence of a healthy heart, the same kidney would perform normally.

New concept: The CRS includes a variety of acute or chronic conditions, where the primary failing organ can be either the heart or the kidney.

Definition

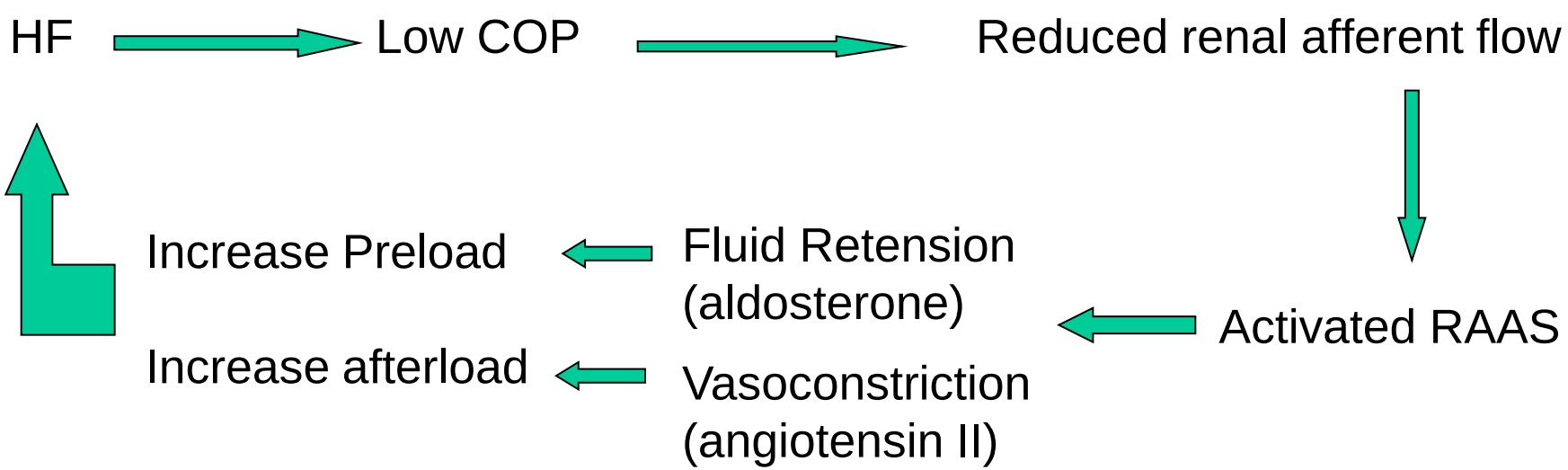
CRS is defined as a pathophysiologic disorder of the heart and kidneys whereby acute or chronic dysfunction of one organ may induce acute or chronic dysfunction of the other.

Classification

CRS Type I (Acute Cardiorenal Syndrome) Abrupt worsening of cardiac function (e.g. acute cardiogenic shock or acutely decompensated congestive heart failure) leading to acute kidney injury
CRS Type II (Chronic Cardiorenal Syndrome) Chronic abnormalities in cardiac function (e.g. chronic congestive heart failure) causing progressive and potentially permanent chronic kidney disease
CRS Type III (Acute Renocardiac Syndrome) Abrupt worsening of renal function (e.g. acute kidney ischaemia or glomerulonephritis) causing acute cardiac disorder (e.g. heart failure, arrhythmia, ischemia)
CRS Type IV (Chronic Renocardiac Syndrome) Chronic kidney disease (e.g. chronic glomerular or interstitial disease) contributing to decreased cardiac function, cardiac hypertrophy and/or increased risk of adverse cardiovascular events
CRS Type V (Secondary Cardiorenal Syndrome) Systemic condition (e.g. diabetes mellitus, sepsis) causing both cardiac and renal dysfunction

Pathophysiology

A) Low flow hypothesis



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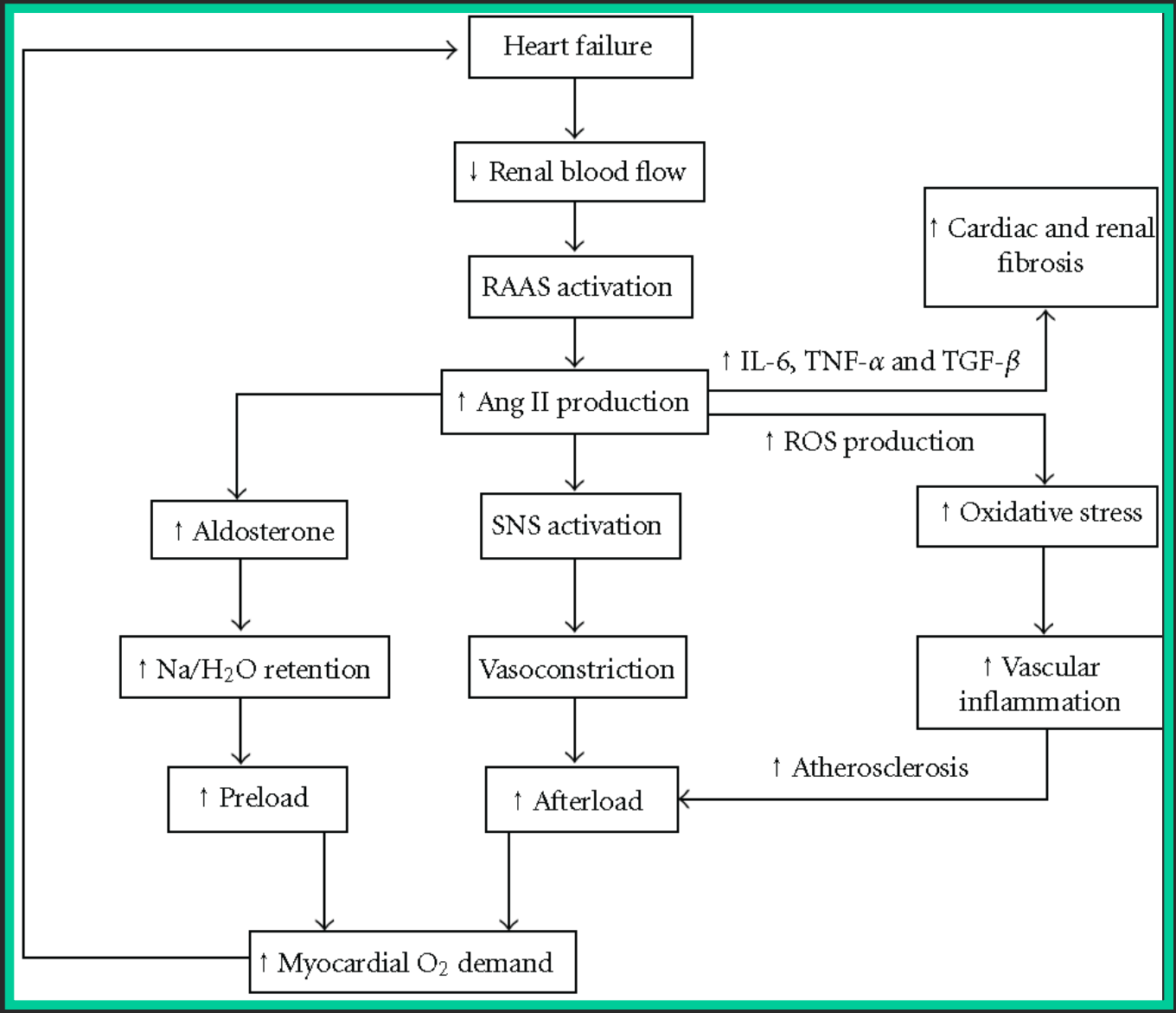
B) Activated RAAS



C) Activated SNS

Activated SNS in HF aims at maintainnig COP by +ve inotropic and chronotropic effect.

SNS activation results in:

- Vasoconstriction → increase afterload
- LVH
- Release of NPY → more atherosclerosis
- Decreased renal blood flow
- Cardiomyocite and Renal tubular cell apoptosis

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D) Systemic congestion

↑ Renal venous pressure → ↓ Glomerular filtration

ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Castheterization Effectiveness) : The only hemodynamic measurement correlated with rising S. cr was Rt. Atrial pressure.

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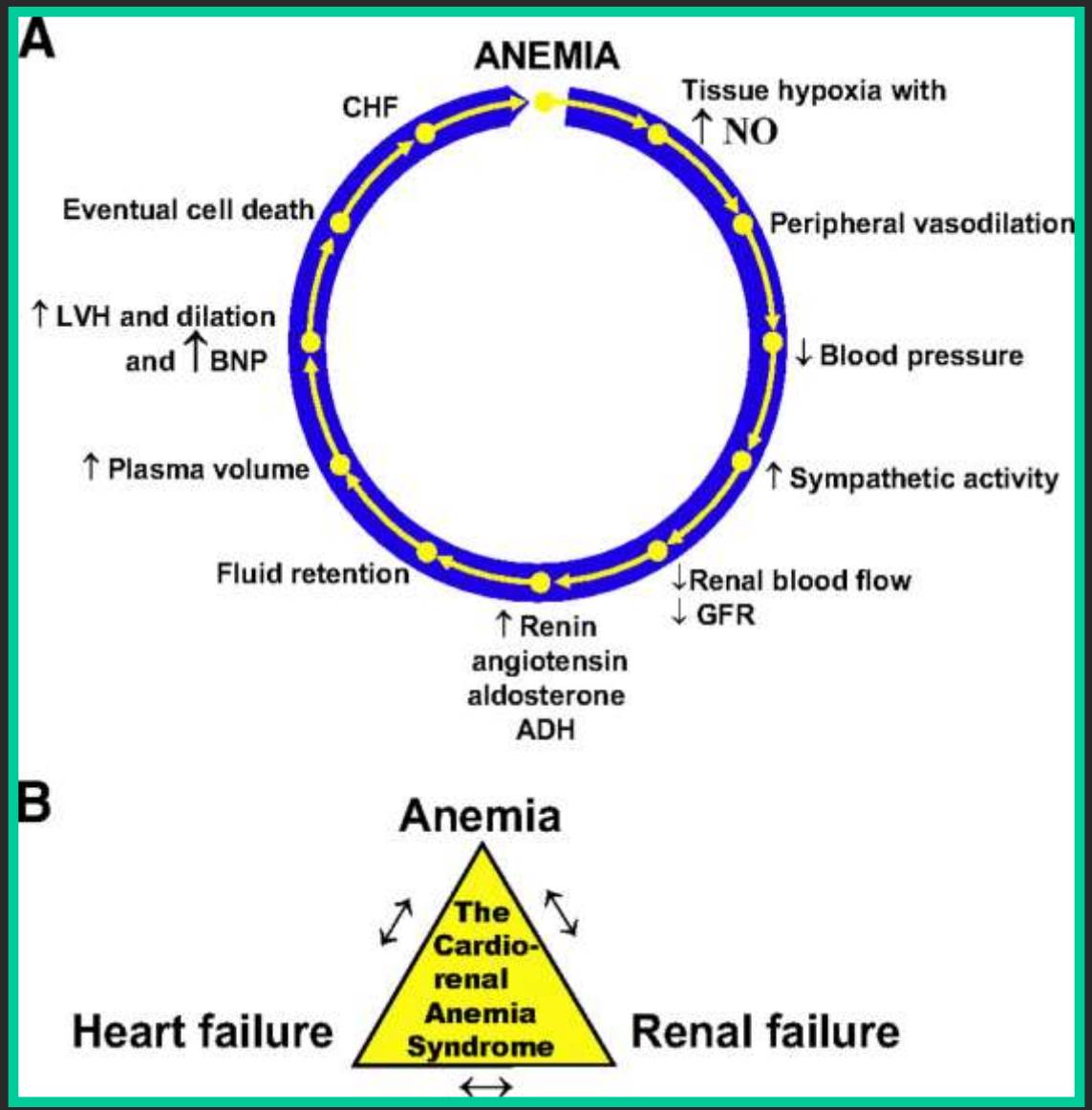
E) CardioRenal Anemia

- Iron Deficiency
- Erythropoietin and ESAs



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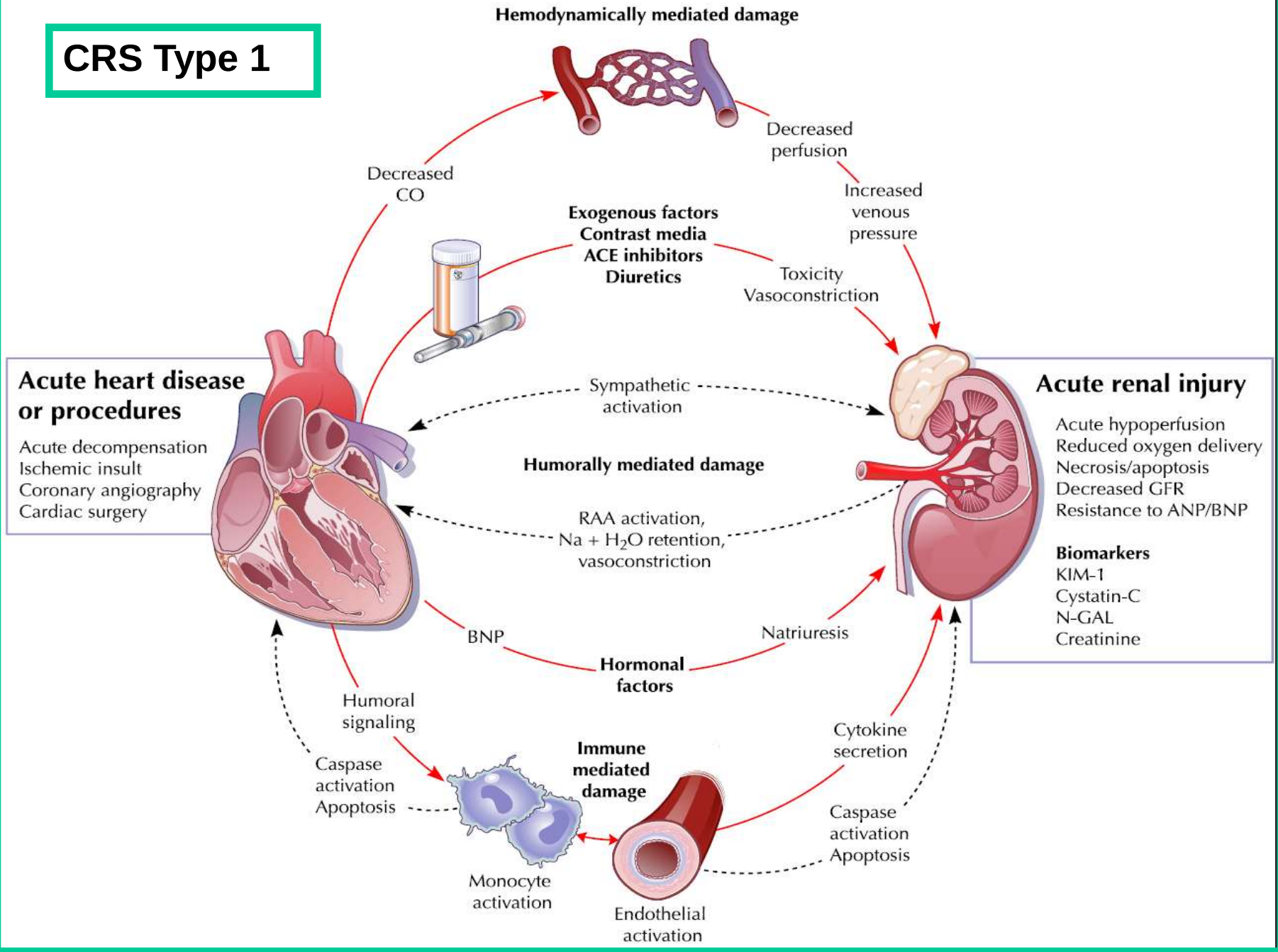
CRS Type 1

- Pathogenesis: Hemodynamics
  Exogenous agents (contrast, diuretics, ACEI)
- Prognostic Factors: EF
  Pre-existing renal disease
- Effect of AKI on the heart: SNS
  RAAS
  Na/H_2O retension
  Inflammation
- Management: Diuretics/ ACEI/BB
- Markers

CRS Type 1


Hemodynamically mediated damage
Decreased perfusion
Increased venous pressure
Toxicity Vasoconstriction
Exogenous factors
Contrast media
ACE inhibitors
Diuretics
Decreased CO
Acute heart disease or procedures
Acute decompensation
Ischemic insult
Coronary angiography
Cardiac surgery
Sympathetic activation
Humorally mediated damage
RAA activation, Na + H_2O retention, vasoconstriction
Acute renal injury
Acute hypoperfusion
Reduced oxygen delivery
Necrosis/apoptosis
Decreased GFR
Resistance to ANP/BNP
Biomarkers
KIM-1
Cystatin-C
N-GAL
Creatinine
BNP
Natriuresis
Hormonal factors
Humoral signaling
Caspase activation Apoptosis
Immune mediated damage
Cytokine secretion
Caspase activation Apoptosis
Monocyte activation
Endothelial activation

Cardio-Renal Syndromes

Table 1 Protein Biomarkers for the Early Detection of Acute Kidney Injury

Biomarker	Associated Injury
Cystatin C	Proximal tubule injury
KIM-1	Ischemia and nephrotoxins
NGAL (lipocalin)	Ischemia and nephrotoxins
NHE3	Ischemia, pre-renal, post-renal AKI
Cytokines (IL-6, IL-8, IL-18)	Toxic, delayed graft function
Actin-actin depolymerizing F	Ischemia and delayed graft function
α-GST	Proximal T injury, acute rejection
π-GST	Distal tubule injury, acute rejection
L-FABP	Ischemia and nephrotoxins
Netrin-1	Ischemia and nephrotoxins, sepsis
Keratin-derived chemokine	Ischemia and delayed graft function

GST = glutathione S-transferase; IL = interleukin; KIM = kidney injury molecule; L-FABP = L-type fatty acid binding protein; NGAL = neutrophil gelatinase-associated lipocalin; NHE = sodium-hydrogen exchanger.

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CRS Type 2

Prevalence : very common 25%

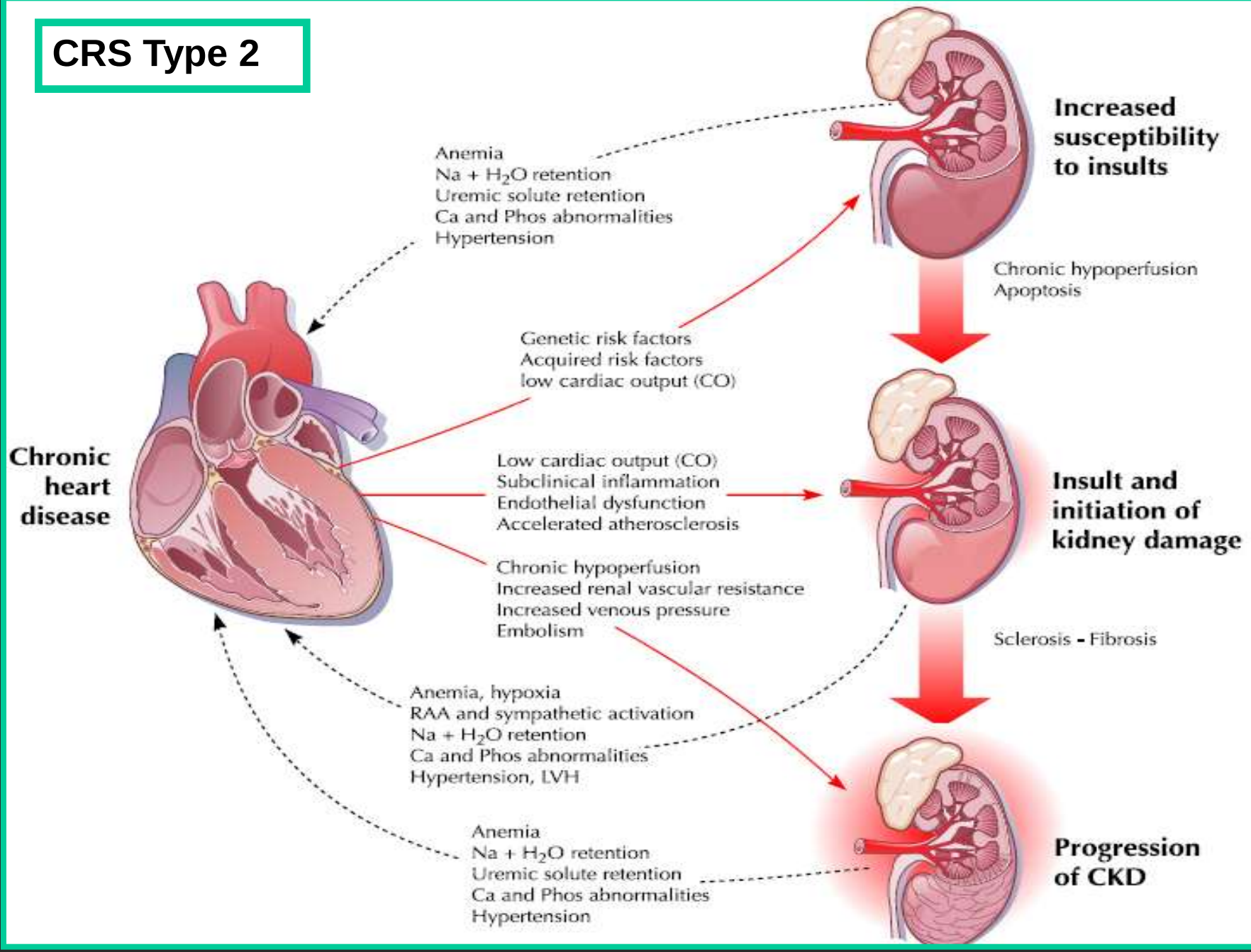
Pathogenesis: Risk Factors
LCOP or Systemic congestion (ESCAPE)
Drugs

Effect of CKI: Anemia / RAAS / Na-H2O / HTN / Uremia

Prognostic Factors: GFR/Age/HTN/DM/ACS

Management: Diuretics
VD drugs
Management of anemia

CRS Type 2


Increased susceptibility to insults
Anemia
Na + H_2O retention
Uremic solute retention
Ca and Phos abnormalities
Hypertension
Chronic hypoperfusion
Apoptosis
Genetic risk factors
Acquired risk factors
low cardiac output (CO)
Chronic heart disease
Low cardiac output (CO)
Subclinical inflammation
Endothelial dysfunction
Accelerated atherosclerosis
Insult and initiation of kidney damage
Chronic hypoperfusion
Increased renal vascular resistance
Increased venous pressure
Embolism
Sclerosis - Fibrosis
Anemia, hypoxia
RAA and sympathetic activation
Na + H_2O retention
Ca and Phos abnormalities
Hypertension, LVH
Anemia
Na + H_2O retention
Uremic solute retention
Ca and Phos abnormalities
Hypertension
Progression of CKD

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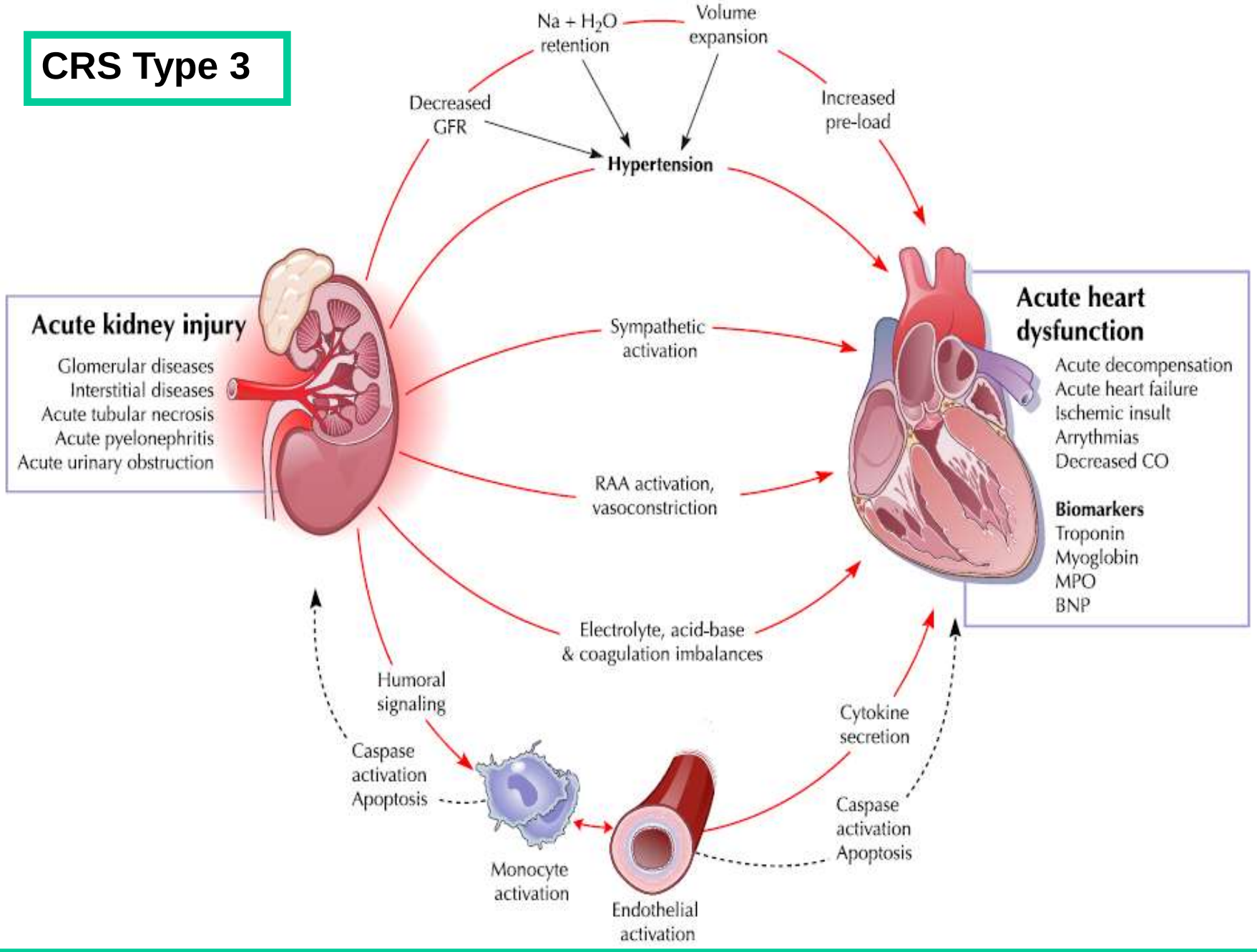
CRS Type 3

Pathogenesis: SNS RAAS
Fluid overload
Electrolytes (hyperkalemia)
Acidemia
Uremia
Bilateral RA stenosis

Biomarkers: Troponins MPO BNP

Management: Diuretics
ACEI
Renal replacement therapy

CRS Type 3


Na + H_2O retention
Volume expansion
Decreased GFR
Increased pre-load
Hypertension
Acute kidney injury
Glomerular diseases
Interstitial diseases
Acute tubular necrosis
Acute pyelonephritis
Acute urinary obstruction
Sympathetic activation
RAA activation, vasoconstriction
Electrolyte, acid-base & coagulation imbalances
Acute heart dysfunction
Acute decompensation
Acute heart failure
Ischemic insult
Arrythmias
Decreased CO
Biomarkers
Troponin
Myoglobin
MPO
BNP
Humoral signaling
Caspase activation Apoptosis
Monocyte activation
Endothelial activation
Cytokine secretion
Caspase activation Apoptosis

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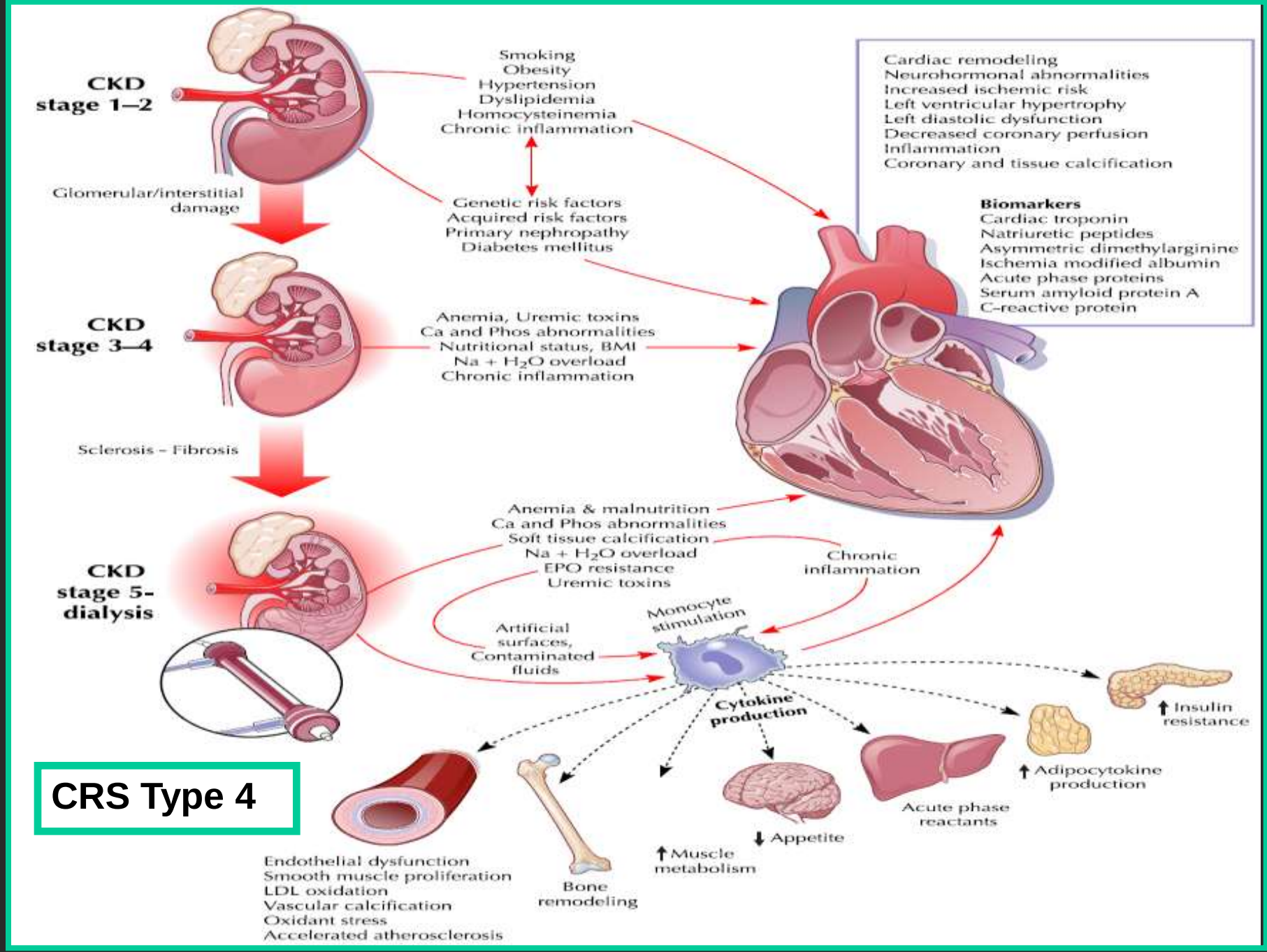
CRS Type 4

Importance: > 50% of CKD V deathes are cardivascular

Pathogenesis: Risk Factors
Anemia
Uremia
Ch. Inflammation
Lack of apropriate CV risk modification treatment

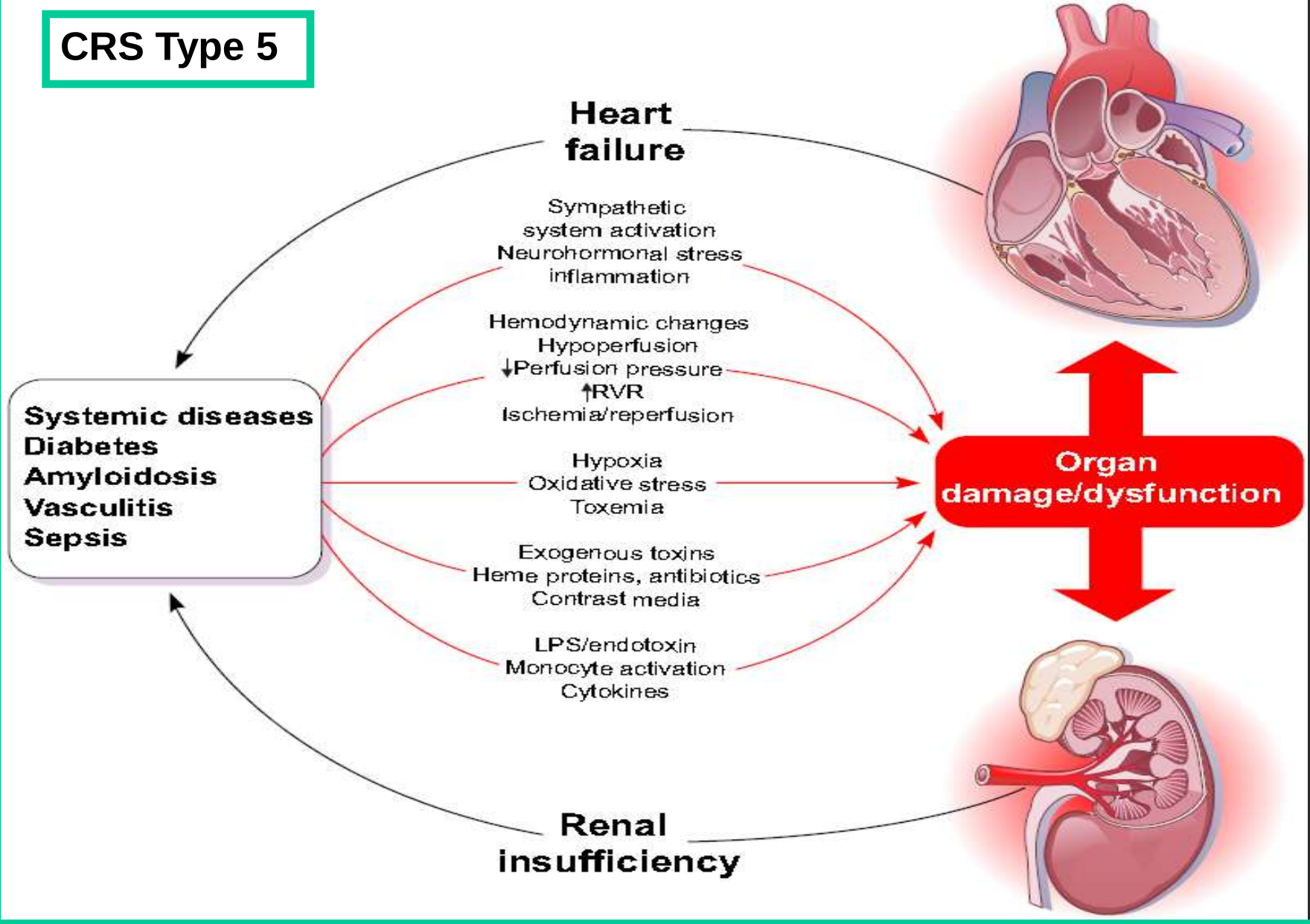
Biomarkers: Troponins
Ischemia modified albumin & Hb
Plasminogen activator inhibitor
BNP, CRP, homocysteine

Management: Antiplatelets, ACEIs, BBs, statins
Endothelin, Adenosine and Vasopressin antagonists


CKD stage 1–2
Smoking
Obesity
Hypertension
Dyslipidemia
Homocysteinemia
Chronic inflammation
Glomerular/interstitial damage
Genetic risk factors
Acquired risk factors
Primary nephropathy
Diabetes mellitus
Cardiac remodeling
Neurohormonal abnormalities
Increased ischemic risk
Left ventricular hypertrophy
Left diastolic dysfunction
Decreased coronary perfusion
Inflammation
Coronary and tissue calcification
Biomarkers
Cardiac troponin
Natriuretic peptides
Asymmetric dimethylarginine
Ischemia modified albumin
Acute phase proteins
Serum amyloid protein A
C-reactive protein
CKD stage 3–4
Anemia, Uremic toxins
Ca and Phos abnormalities
Nutritional status, BMI
Na + H2O overload
Chronic inflammation
Sclerosis – Fibrosis
CKD stage 5-dialysis
Anemia & malnutrition
Ca and Phos abnormalities
Soft tissue calcification
Na + H2O overload
EPO resistance
Uremic toxins
Chronic inflammation
Monocyte stimulation
Artificial surfaces, Contaminated fluids
Cytokine production
Insulin resistance
Adipocytokine production
Acute phase reactants
Appetite
Muscle metabolism
Bone remodeling
Endothelial dysfunction
Smooth muscle proliferation
LDL oxidation
Vascular calcification
Oxidant stress
Accelerated atherosclerosis

CRS Type 4

CRS Type 5


Heart failure
Sympathetic system activation
Neurohormonal stress
inflammation
Hemodynamic changes
Hypoperfusion
↓Perfusion pressure
↑RVR
Ischemia/reperfusion
Hypoxia
Oxidative stress
Toxemia
Exogenous toxins
Heme proteins, antibiotics
Contrast media
LPS/endotoxin
Monocyte activation
Cytokines
Systemic diseases
Diabetes
Amyloidosis
Vasculitis
Sepsis
Organ damage/dysfunction
Renal insufficiency

THANK YOU